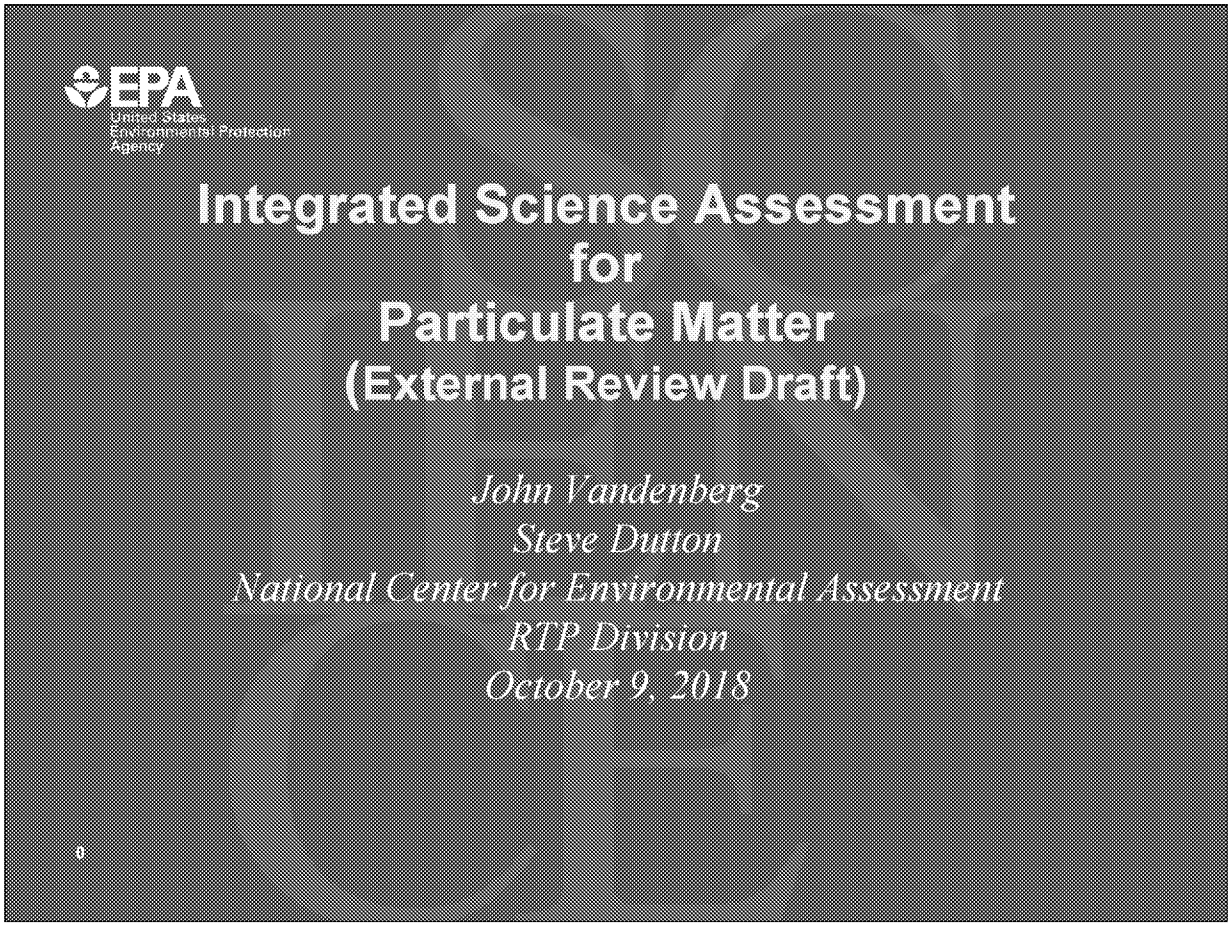
EPA
United States
Environmental Protection
Agency
Integrated Science Assessment
for
Particulate Matter
(External Review Draft)
John Vandenberg
Steve Dutton
National Center for Environmental Assessment
RTP Division
October 9, 2018
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NCEA/ORD and OAQPS/OAR Interactions: NAAQS Review

NCEA/ORD	NAAQS Activity	OAQPS/OAR
Co-lead development of workshop	**Workshop on science-policy issues (ORD/OAR)**	Co-lead development of workshop
Author – Chapter on ISA	**Integrated Review Plan (ORD/OAR)**	Author of other chapters (e.g., REA, PA)
Lead development	**Integrated Science Assessment (ORD)**	Review draft materials with focus on identifying areas where clarification is needed
Review draft materials and provide comments on interpretation of science	**Risk/Exposure Assessment (OAR)**	Lead development
Review draft materials and provide comments on interpretation of science	**Policy Assessment (OAR)**	Lead development
Provide technical and scientific support	**Rule-making materials (OAR)**	Lead development

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Scope of PM ISA

- **Scope:** The ISA is tasked with answering the question "Is there an independent effect of PM on health and welfare at relevant ambient concentrations?"
  - Health Effects
    - Studies will be considered if they include a composite measure of PM (e.g., $PM_{2.5}$ mass, $PM_{10-2.5}$ mass, ultrafine particle (UFP) number)
      - Studies of source-based exposures that contain PM (e.g., diesel exhaust, wood smoke, etc.) if they have a composite measure of PM and examine effects with and without particle trap to assess the particle effect
      - Studies of components of PM if they include a composite measure of PM to relate toxicity of component(s) to current indicator
    - Studies will be considered if PM exposures are relevant to ambient concentrations (< 2 mg/m^3; 1 to 2 orders of magnitude above ambient concentrations)

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Scope of PM ISA (cont.)

- Welfare Effects
  - Focus is on non-ecological welfare effects
    - Visibility Impairment
    - Climate Effects
    - Materials Effects
  - Ecological effects resulting from the deposition of PM and PM components are being considered as part of the review of the secondary (welfare-based) NAAQS for oxides of nitrogen, oxides of sulfur and PM

PM ISA: Overall Observations

- Systematic Review of PM Literature Base
  - Initial search identified ~310,000; ~5,100 read past the title with 2,655 cited in the ISA
- $PM_{2.5}$
  - Expansive body of literature supports and extends the conclusions of 2009 PM ISA
  - More extensive evaluation of some "newer" health effects (nervous system and metabolic)
  - Extensive analyses across health effects continues to support linear, no-threshold concentration-response (C-R) relationship
  - Effects observed at long-term average concentrations below the current annual standard
- $PM_{10-2.5}$
  - Relatively fewer studies examine health effects due to $PM_{10-2.5}$ exposures
  - Uncertainties still remain with respect to differences in methods used in epidemiology studies for estimation of $PM_{10-2.5}$ concentrations across studies
- Ultrafine Particles (UFP)
  - Variability in size distribution and exposure metric examined across studies
  - Majority of epidemiologic studies conducted outside U.S., most relying on 1 monitor
  - Lack of U.S. monitoring network and limited data on spatial and temporal UFP concentrations, particularly in the U.S.

Contents of the Draft PM ISA

Preface: Legislative Requirements of the PM NAAQS, Purpose and Overview of the ISA, Process for Developing ISA

Executive Summary

Chapter 1. Integrated Synthesis

Chapter 2. Sources, Atmospheric Chemistry, and Ambient Concentrations

Chapter 3. Exposure to Ambient PM

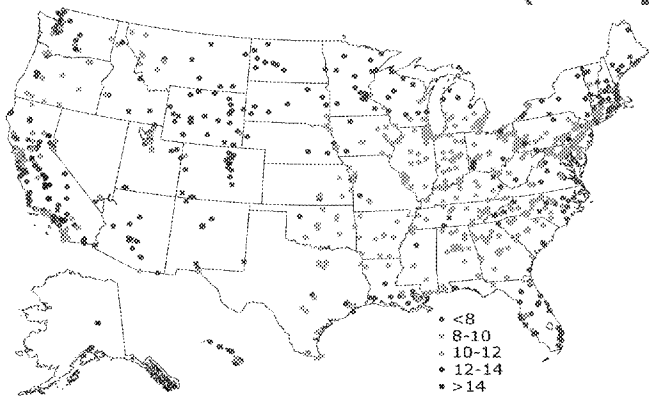
Chapter 4. Dosimetry of PM

Chapters 5 - 11. Respiratory Effects, Cardiovascular Effects, Metabolic Effects, Nervous System Effects, Reproductive and Developmental Effects, Cancer, and Mortality

Chapter 12. Lifestages and Populations Potentially at Increased Risk of a PM-related Health Effect

Chapter 13. Welfare Effects

$PM_{2.5}$ Concentrations and Trends (Chapter 2)



- Highest average and 98th percentile in California
- Steady declining trend from 2000 to 2015
- Summer no longer has the highest $PM_{2.5}$ concentrations nationally
- Annual average decreased from 12 µg/m³ to 8.6 µg/m³ from 2006 to 2014

Figure 2-13. Three-year average $PM_{2.5}$ concentrations 2013–2015 (µg/m³)

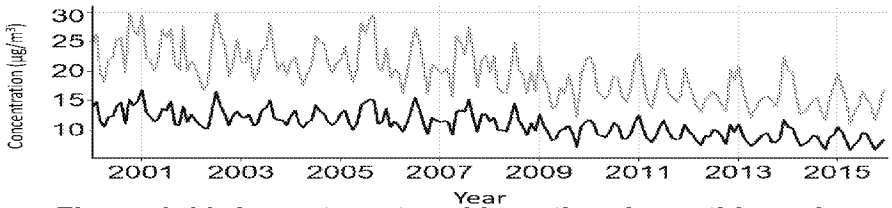


Figure 2-22. Long-term trend in national monthly and annual average $PM_{2.5}$ concentrations (µg/m³) from 2000–2015

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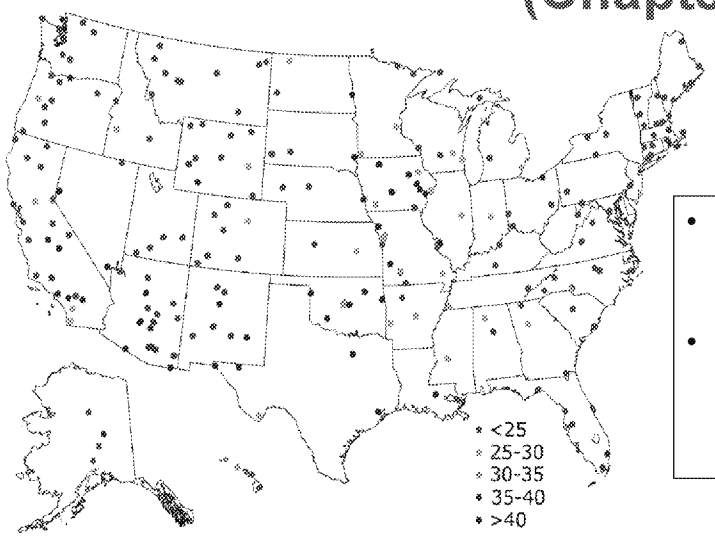
$PM_{10-2.5}$ Concentrations and Trends (Chapter 2)



- Highest $PM_{10-2.5}$ concentrations in California, Southwest, High Plains
- Recent data indicates that the contribution of $PM_{10-2.5}$ to PM_{10} is higher than previously reported

Figure 2-16. 98th percentile concentrations $PM_{10-2.5}$ concentrations 2013−2015 (µg/m³)

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UFP Concentrations and Trends (Chapter 2)

- Ultrafine particles are generally considered to be PM with a diameter less than or equal to 0.1 µm (100 nm)
- Uncertainties:
  - Highly variable concentration in space and over time due to physical and chemical processing in the atmosphere
    - UFP concentrations are highest in urban areas and during rush hour, and are highly episodic during winter
  - UFP measured using multiple methods, varying in the size ranges examined - some capturing multiple size ranges below 100 nm, while others can include sizes above 100 nm
- Number of U.S. sites with routine monitoring of UFP has increased from 3 in 2015 to 23 in 2018

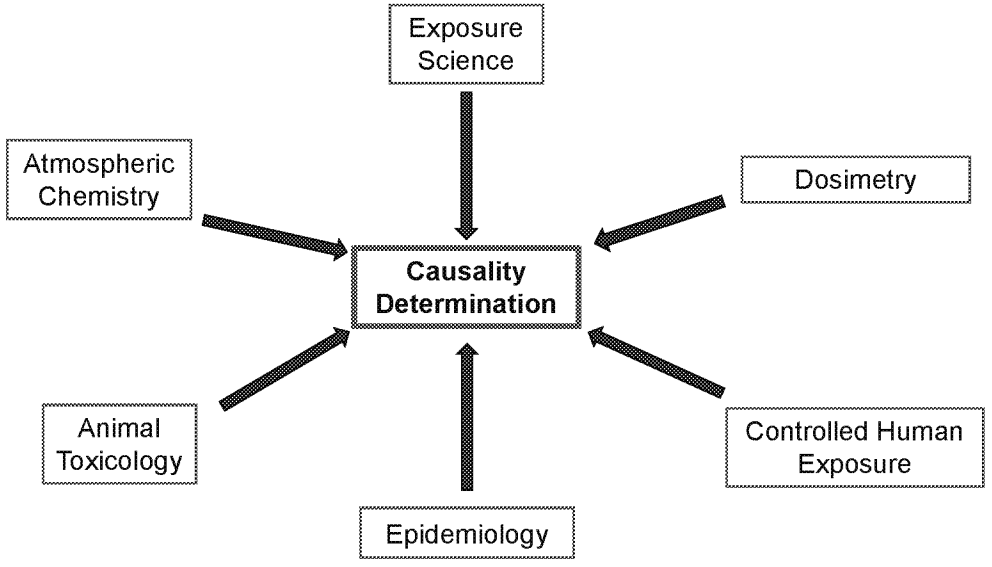
Exposure to PM (Chapter 3)

Method	Epidemiologic Application: Short-term	Epidemiologic Application: Long-term	Potential Errors and Uncertainties
Fixed-site monitors	X		Correlation between exposure and measurement decreases with increasing distance from the monitor, especially for $PM_{10-2.5}$ and UFP
		X	Errors in $PM_{10-2.5}$ concentrations related to different flow rates used in PM_{10} and $PM_{2.5}$ monitors for the differencing methods Errors in $PM_{10-2.5}$ concentrations due to differences in locations of PM_{10} and $PM_{2.5}$ monitors when the instruments are not collocated Exposure misclassification if the monitor site does not correspond to the exposed population
Land-use regression and spatio-temporal models		X	Exposure misclassification if grid is not finely resolved Bias if the model is misspecified or applied to a location different from where the model was fit
Chemical transport model		X	Bias when grid cells are too large to capture spatial variability of ambient PM exposures, especially for $PM_{10-2.5}$ Bias in PM mass concentration and PM components related to underestimation of BC and OC
Satellite-based methods		X	Bias when grid cells are too large to capture spatial variability of ambient PM exposures, especially for $PM_{10-2.5}$
Hybrid models		X	Bias when grid cells are too large to capture spatial variability of ambient PM exposures, especially for $PM_{10-2.5}$ Bias in PM mass concentration and PM components related to underestimation of BC and OC, reduced by monitor and/or satellite data

Dosimetry of PM (Chapter 4)

- New information in this review:
  - Demonstrates that children inhale less through the nose and have lower nasal deposition efficiency than adults resulting in increased exposure of the lungs to inhaled PM
  - Shows the translocation of a small fraction of particles (≤ 0.2 μm) out of the respiratory tract from the:
    - Olfactory mucosa to the brain
    - Alveolar region of the lung into blood
  - Indicates that PM_{10} overestimates the size of particles likely to enter the human lung

Evidence Base that Informs Health-Based Causality Determinations



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Draft PM ISA
Health Effects: Causality Determinations

HUMAN HEALTH EFFECTS

Health Outcome			ISA	Current PM Draft ISA		
			Indicator	$PM_{2.5}$	$PM_{10-2.5}$	UFP
	Mortality		Short-term exposure		*	
			Long-term exposure		*	
	Respiratory		Short-term exposure			
			Long-term exposure			
	Cardiovascular		Short-term exposure			
			Long-term exposure		*	
	Metabolic		Short-term exposure	*	*	*
			Long-term exposure	*	*	*
	Reproductive	Male/Female Reproduction and Fertility	Long-term exposure			
		Pregnancy and Birth Outcomes				
	Cancer		Long-term exposure	*	*	
	Central nervous system		Short-term exposure	*		*
			Long-term exposure	*	*	*

Causal | Likely causal | Suggestive | Inadequate

* = new determination or change in causality determination from 2009 PM ISA

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Example: Organizational Structure of Health Effects Chapters

- Text Box: Overview of causality determinations
- Short-term $PM_{2.5}$ Exposure
  - Biological plausibility discussion and figure
  - Evaluation of the health effects evidence by broad health effects (e.g., myocardial infarction, asthma)
  - Evaluation of components and sources evidence
  - Summary and Causality determination
- Long-term $PM_{2.5}$ Exposure
  - Biological plausibility discussion and figure
  - Evaluation of the health effects evidence by broad health effects (e.g., myocardial infarction, asthma)
  - Evaluation of components and sources evidence
  - Summary and Causality determination
- Similar structure for $PM_{10-2.5}$ and ultrafine particle (UFP) sections

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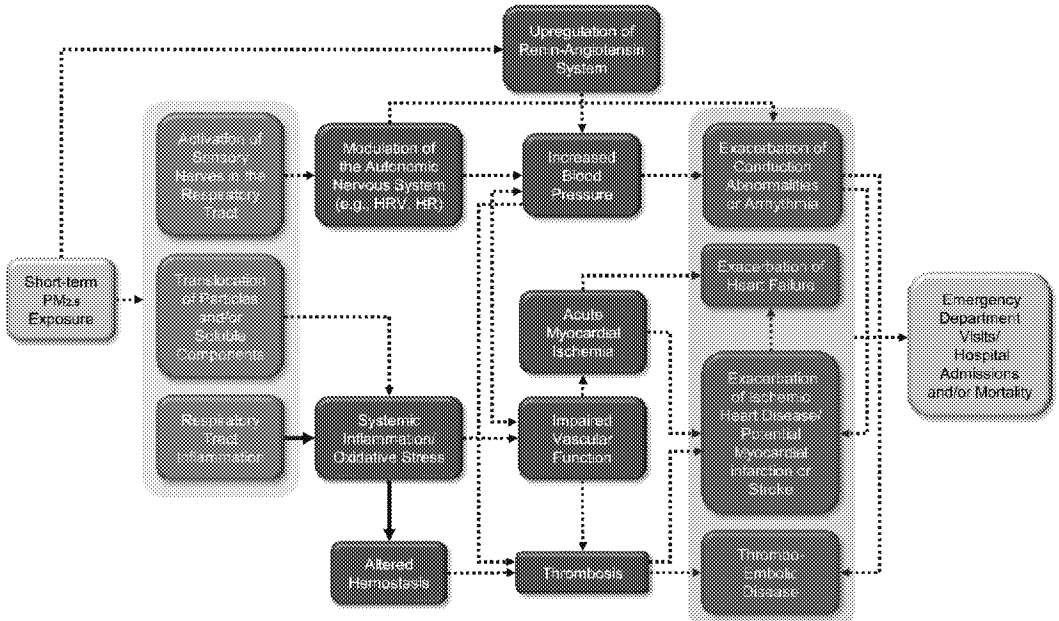
Example: Potential Biological Pathways Figure



Note: The boxes above represent the effects for which there is experimental or epidemiologic evidence, and the dotted arrows indicate a proposed relationship between those effects. Solid arrows denote direct evidence of the relationship as provided, for example, by an inhibitor of the pathway or a genetic knock-out model used in an experimental study. Shading around multiple boxes denotes relationships between groups of upstream and downstream effects. Progression of effects is depicted from left to right and color-coded (gray, exposure; green, initial event; blue, intermediate event; orange, apical event). Here, apical events generally reflect results of epidemiologic studies, which often observe effects at the population level. Epidemiologic evidence may also contribute to upstream boxes. When there are gaps in the evidence, there are complementary gaps in the figure.

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Respiratory Effects (Chapter 5)

Recent evidence supports the conclusions of the 2009 PM ISA, and continues to support a likely to be causal relationship between short- and long-term $PM_{2.5}$ exposure and respiratory effects

- Short-term $PM_{2.5}$ Exposure **(Likely to be Causal)**
  - Epidemiologic evidence: consistent evidence for asthma exacerbation in children and COPD exacerbation in adults, as well as respiratory mortality.
    - Recent studies examining potential copollutant confounding provide evidence supporting an independent $PM_{2.5}$ effect, particularly for asthma exacerbation and respiratory mortality
  - Experimental evidence: worsening of allergic airways disease and/or subclinical effects related to COPD, provide biological plausibility for asthma and COPD exacerbations
- Long-term $PM_{2.5}$ Exposure **(Likely to be Causal)**
  - Epidemiologic evidence: consistent changes in lung function and lung function growth rate, increased asthma incidence, asthma prevalence and wheeze in children; acceleration of lung function decline in adults; and respiratory mortality
    - Independent $PM_{2.5}$ effect supported by examination of potential copollutant confounding, particularly studies of lung function growth and respiratory mortality; improvements in lung function growth with declining $PM_{2.5}$ concentrations
  - Experimental evidence: impaired lung development and development of allergic airways disease, biological plausibility for decrements in lung function growth in children and asthma development

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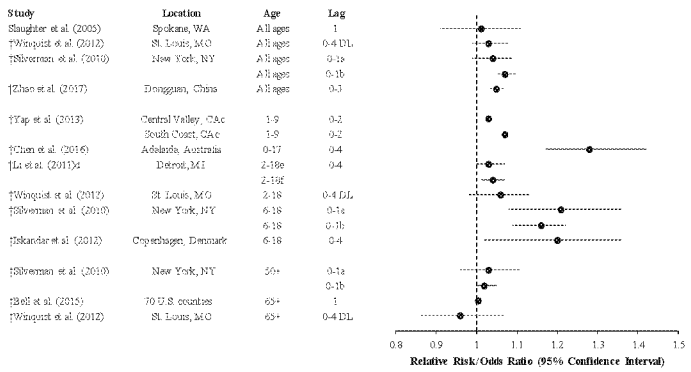
Respiratory Effects (Chapter 5)

Example: Short-term $PM_{2.5}$ Exposure and Asthma

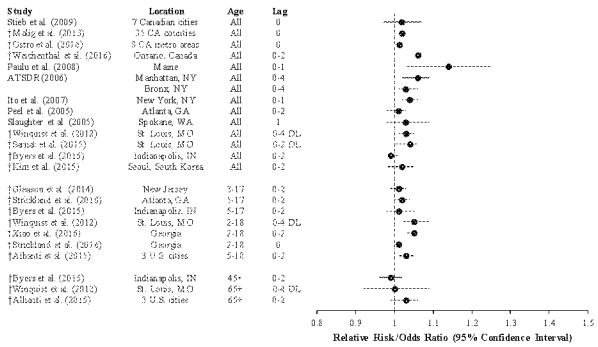


Hospital Admissions

Red = recent studies;
Black = U.S. study evaluated in the 2009 PM ISA

Emergency Department Visits

Red = recent studies;
Black = U.S. and Canadian studies evaluated in the 2009 PM ISA



Cardiovascular Effects (Chapter 6)

A large body of recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between short- and long-term $PM_{2.5}$ exposure and cardiovascular effects

- Short-term $PM_{2.5}$ Exposure **(Causal)**
  - Epidemiologic evidence: generally consistent positive associations for hospital admissions and ED visits, particularly for ischemic heart disease (IHD) and heart failure (HF), as well as cardiovascular mortality
  - Experimental evidence: endothelial dysfunction, effects indicating impaired cardiac function, arrhythmia, changes in heart rate variability (HRV), increases in blood pressure (BP), and indicators of systemic inflammation, oxidative stress, and coagulation
- Long-term $PM_{2.5}$ Exposure **(Causal)**
  - Epidemiologic evidence: consistent positive associations for cardiovascular mortality; evidence for coronary heart disease (CHD) and stroke particularly in populations with pre-existing disease; evidence for coronary artery calcification (CAC)
    - Cardiovascular mortality studies inform potential copollutant confounding, and linear, no-threshold concentration-response relationship
  - Experimental evidence: impaired heart function, increased blood pressure, endothelial dysfunction, and atherosclerotic plaque progression

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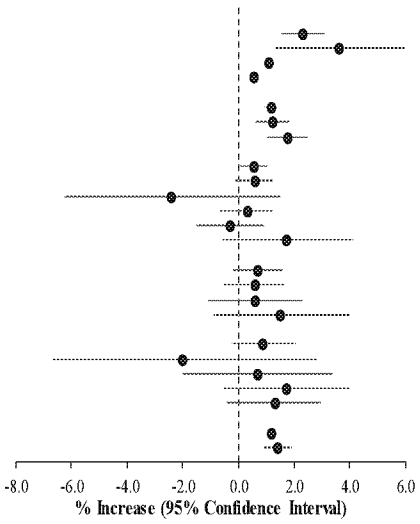
Cardiovascular Effects (Chapter 6)

Example: Short-term $PM_{2.5}$ Exposure and Cardiovascular-related Mortality

Study	Location	Lag	Outcome
†Lee et al. (2015)a	3 Southeast states, U.S.	0-1	Cardiovascular
			CHF
			MI
			Stroke
†Dai et al. (2014)	75 U.S. cities	0-1	Cardiovascular
			MI
			Stroke
†Samoli et al. (2013)	10 European Med cities	0-1	Cardiovascular
†Samoli et al. (2014)	10 European Med cities		Cardiac
			CHF
			Cerebrovascular
			Acute Coronary Events
			Arrhythmias
†Pascal et al. (2014)	9 French cities	0-1	Cardiovascular
			Cardiac
			IHD
			Cerebrovascular
†Milojevic et al. (2014)	England and Wales	0-1	Cardiovascular
			CHF
			MI
			Stroke
			IHD
†Shah et al. (2015)	Meta-analysis	---	Stroke
†Wang et al. (2014)	Meta-analysis	---	Stroke



Red = recent studies

Figure 6-7. Percent increase in cause-specific cardiovascular mortality outcomes for a 10 µg/m³ increase in 24-hour average $PM_{2.5}$ concentrations observed in multicity studies and meta-analyses.

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Nervous System Effects (Chapter 8)

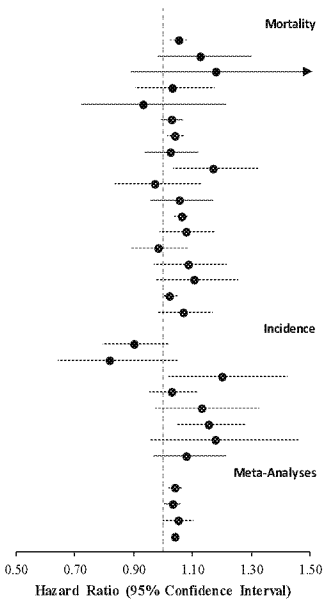
- Long-term $PM_{2.5}$ Exposure **(Likely to be Causal – NEW conclusion)**
  - Epidemiologic evidence
    - Consistent evidence for cognitive decline/impairment and decreased brain volume; more limited evidence for Alzheimer's disease and dementia
    - Lack of examination of potential copollutant confounding
  - Experimental evidence
    - Consistent evidence for inflammation, oxidative stress, morphologic changes, and neurodegeneration in multiple brain regions of adult animals
    - Limited evidence for early indicators of Alzheimer's disease, impaired learning/memory, altered behavior in adult animals, and morphologic changes during development
    - Evidence supports biological plausibility for cognitive decrements and dementia, and independent $PM_{2.5}$ effect
- Long-term UFP Exposure **(Likely to be Causal – NEW conclusion)**
  - Epidemiologic evidence
    - Limited evidence for effects on cognitive development in children
  - Experimental evidence
    - Consistent evidence for inflammation, oxidative stress, and neurodegeneration in adult animals
    - Limited evidence of Alzheimer's disease pathology in a susceptible animal model
    - Strong evidence, mainly from one laboratory, for inflammation, morphologic changes including persistent ventriculomegaly, and behavioral effects following pre/postnatal exposure

Cancer (Chapter 10)

- Long-term $PM_{2.5}$ Exposure **(Likely to be Causal – NEW conclusion)**
  - Recent epidemiologic studies greatly expand upon the limited number of studies in the 2009 PM ISA that examined lung cancer incidence and mortality
    - Primarily positive associations, supported by analyses focusing on never smokers
  - Experimental and epidemiologic studies provide evidence for a relationship between $PM_{2.5}$ exposure and genotoxicity, epigenetic effects, and carcinogenic potential.
  - $PM_{2.5}$ exhibits several characteristics of carcinogens providing biological plausibility for $PM_{2.5}$ exposure contributing to cancer development

Cancer (Chapter 10)

Study	Cohort	Location	Follow-up Years	Qualifier
Krewski et al. (2009)	ACS (Re-analysis)	U.S.	1982-2000	
Laden et al. (2006)	HSC	6 U.S. cities	1974-1998	
McDonnell et al. (2000)	AHSMOG	California	1973-1977	Men
Brunekreef et al. (2009)a	NLCS - Air	Netherlands	1987-1996	Full Cohort
Brunekreef et al. (2009)a	NLCS - Air	Netherlands	1987-1996	Case Cohort
†Thurston et al. (2013)	ACS-CPS II	U.S.	1982-2004	
†Turner et al. (2016)	ACS-CPS II	U.S.	1982-2004	
†Hart et al. (2011)	TrIPS	U.S.	1985-2000	Men
†Lepeule et al. (2012)	HSC	6 U.S. cities	1974-2009	
†Lipsett et al. (2011)	CTS	California	2000-2005	Women
†Jerrett et al. (2013)	ACS-CPS II	California	1982-2000	
†Crouse et al. (2015)	CanCHEC	Canada	1991-2006	
†Pinault et al. (2016)	CCHS	Canada	2000-2011	
†Villeneuve et al. (2015)	CNBSS	Canada	1980-2005	Women
†Weichenthal et al. (2016)	CanCHEC	Ontario	1991-2009	
†Carey et al. (2013)	National English	United Kingdom	2003-2007	
†Cesaroni et al. (2013)	RoLS	Rome, Italy	2001-2010	
†Wong et al. (2016)	---	Hong Kong	1998-2011	
Brunekreef et al. (2009)b	NLCS - Air	Netherlands	1987-1996	Full Cohort
Brunekreef et al. (2009)b	NLCS - Air	Netherlands	1987-1996	Case Cohort
†Gharibvand et al. (2016)	AHSMOG-2	U.S.	2002-2011	
†Puett et al. (2014)	NHS	U.S.	1994-2010	Women
†Hystad et al. (2013)	MECSS	Canada	1994-1997	
†Tomczak et al. (2016)	CNBSS	Canada	1980-2004	Women
†Raaschou-Nielsen et al. (2013)	ESCAPE	Europe	1990s	
†Hart et al. (2015)	NCLS	Netherlands	1986-2003	
†Hamra et al. (2014)c	---	---	---	14 studies
†Yang et al. (2015)c	---	---	---	10 studies
†Chen et al. (2015)c	---	---	---	6 studies
†Cui et al. (2015)d	---	---	---	12 studies



Note: Red = recent studies; Black = studies evaluated in the 2009 PM ISA

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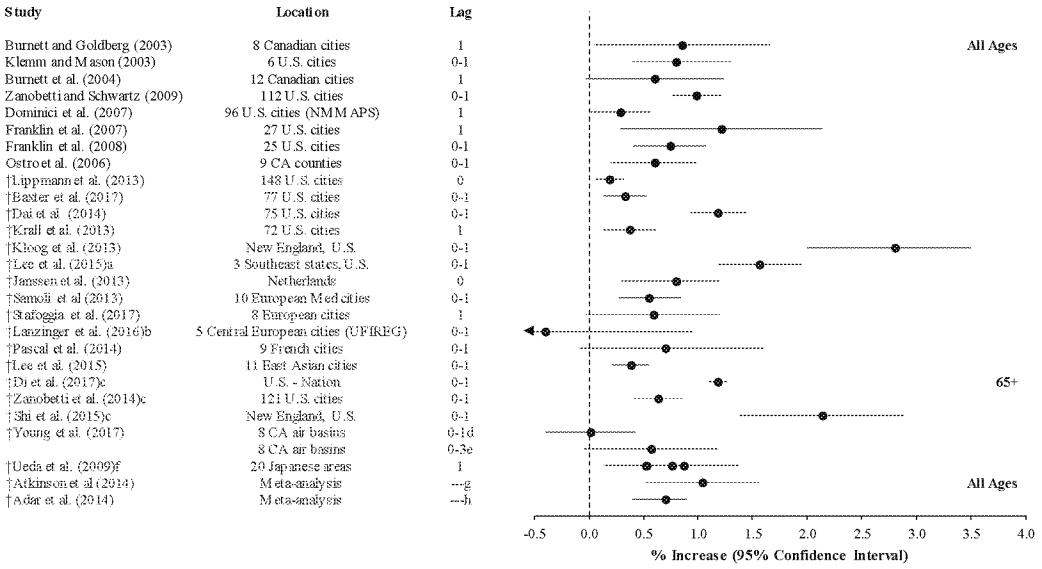
Figure 10-3. Summary of associations reported in previous and recent cohort studies that examined long-term $PM_{2.5}$ exposure and lung cancer mortality and incidence.

Mortality – Short-term $PM_{2.5}$ Exposure (Chapter 11) (Causal)

Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between short-term $PM_{2.5}$ exposure and mortality



Note: Red = recent multi-city studies; Black = multi-city studies evaluated in the 2009 PM ISA

Figure 11-1. Summary of associations between short-term PM2.5 exposure and total (nonaccidental) mortality in multicity studies for a 10 µg/m^3 increase in 24-hour average concentrations.

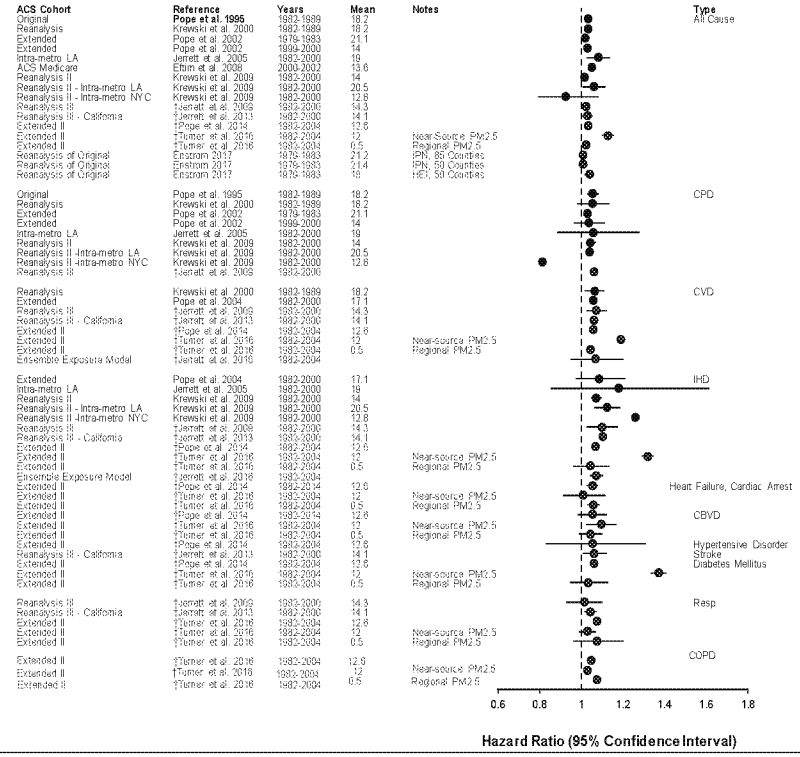
Mortality – Long-term $PM_{2.5}$ Exposure (Chapter 11) (Causal)

Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between long-term $PM_{2.5}$ exposure and mortality

Figure 11-17. Associations between long-term exposure to $PM_{2.5}$ and total (nonaccidental) mortality in the American Cancer Society (ACS) cohort.

Note: Associations are presented per 5 µg/m³ increase in pollutant concentration.

Red = recent studies;
Black = studies evaluated in the 2009 PM ISA



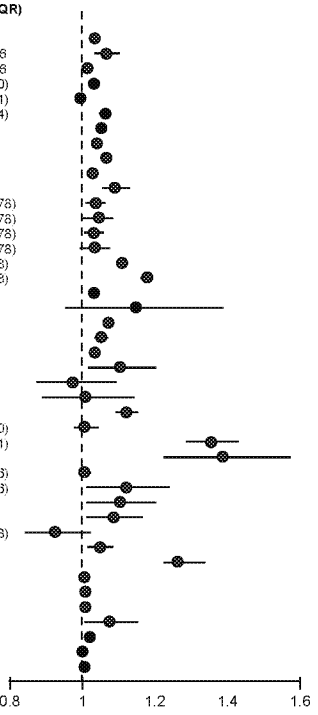
Mortality – Long-term $PM_{2.5}$ Exposure (Chapter 11) (Causal)

Figure 11-18. Associations between long-term $PM_{2.5}$ and total (nonaccidental) mortality in recent North American cohorts.

Note: Associations are presented per 5 μg/m³ increase in pollutant concentration.

Red = recent studies;
Black = studies evaluated in the 2009 PM ISA

Reference	Cohort	Notes	Years	Mean (IQR)
†Pope et al. 2014	ACS		1982-2004	12.8
†Lepeule et al. 2012	Harvard Six Cities		1974-2009	11.4-23.6
†Thurston et al. 2015	NIH-AARP		2000-2009	10.2-13.6
Zeger et al. 2008	MCAPS	Eastern	2000-2005	14.0 (3.0)
Zeger et al. 2008	MCAPS	Western	2000-2005	13.1 (8.1)
Zeger et al. 2008	MCAPS	Central	2000-2005	10.7 (2.4)
Eftim et al. 2008	ACS-Medicare		2000-2002	13.6
†Di et al. 2017	Medicare		2000-2012	11.5
†Di et al. 2017	Medicare	exp<12	2000-2012	11.5
†Di et al. 2017	Medicare	nearest monitor	2000-2012	11.5
†Kioumourtzoglou et al. 2016	Medicare		2000-2010	12
†Shi et al. 2015	Medicare	mutual adj	2003-2008	8.12 (3.78)
†Shi et al. 2015	Medicare	exp <10, mutual adj	2003-2008	8.12 (3.78)
†Shi et al. 2015	Medicare	no mutual adj	2003-2008	8.12 (3.78)
†Shi et al. 2015	Medicare	exp <10, no mutual adj	2003-2008	8.12 (3.78)
†Wang et al. 2017	Medicare		2000-2013	10.7 (3.8)
†Wang et al. 2017	Medicare	exp<12	2000-2013	10.7 (3.8)
Lipfert et al. 2006	Veterans Cohort		1997-2001	14.34
Goss et al. 2004	U.S. Cystic Fibrosis		1999-2000	13.7
†Crouse et al. 2012	CanCHEC	Satellite data	1991-2001	8.9
†Crouse et al. 2012	CanCHEC	Monitor data	1991-2001	11.2
†Crouse et al. 2015	CanCHEC		1991-2006	8.9
†Chen et al. 2016	EFFECT		1999-2011	10.7
†Weichenthal et al. 2014	Ag Health		1993-2009	8.84
†Weichenthal et al. 2014	Ag Health	more precise exp	1993-2009	8.84
†Pinault et al. 2016	CCHS		1998-2011	8.3
†Lipsett et al. 2011	CA Teachers		2000-2005	15.6 (8.0)
†Ostro et al. 2010	CA Teachers	within 30 km	2002-2007	17.5 (6.1)
†Ostro et al. 2010	CA Teachers	within 8 km	2002-2007	17 (6.1)
†Ostro et al. 2015	CA Teachers		2001-2007	17.9 (9.6)
†Puett et al. 2009	Nurses Health		1992-2002	13.9 (3.6)
†Hart et al. 2015	Nurses Health	nearest monitor	2000-2006	12.7
†Hart et al. 2015	Nurses Health	spatio-temp. model	2000-2006	12
†Puett et al. 2011	Health Prof	full model	1989-2003	17.8 (4.3)
†Hart et al. 2011	TrIPS		1985-2000	14.1 (4)
†Kloog et al. 2013	MA cohort	CVD+Resp	2000-2008	9.9 (1.6)
†Garcia et al. 2015	CA cohort	Kriging	2006	13.06
†Garcia et al. 2015	CA cohort	IDW	2006	12.94
†Garcia et al. 2015	CA cohort	closest monitor	2006	12.68
†Wang et al. 2016	NJ Cohort		2004-2009	11.3
Enstrom 2005	CA Cancer Prev		1973-1982	23.4
Enstrom 2005	CA Cancer Prev		1983-2002	23.4
Enstrom 2005	CA Cancer Prev		1973-2002	23.4



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Policy-Relevant Considerations: Potential Copollutant Confounding

Across recent studies examining various health effects and both short- and long-term $PM_{2.5}$ exposures, associations remain relatively unchanged in copollutant models

- In the 2009 PM ISA an overall limitation of the epidemiologic evidence spanning health effects was the rather limited assessment of potential copollutant confounding
- Recent epidemiologic studies greatly expand upon this limitation by conducting copollutant analyses with gaseous as well as other particle size fractions (i.e., $PM_{10-2.5}$)

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Policy-Relevant Considerations: PM Components and Sources

Many $PM_{2.5}$ components and sources are associated with many health effects, and the evidence does not indicate that any one source or component is more strongly related with health effects than $PM_{2.5}$ mass

- Evaluation of PM components focused on studies that examined both PM components and a composite metric of PM
  - Most studies in the current literature focus on $PM_{2.5}$ components
- Evaluation of PM sources focused on studies that used statistical approaches to attribute specific $PM_{2.5}$ components to sources
- Across the evidence spanning health categories (e.g., cardiovascular effects, mortality) and various health effects (e.g., hospital admissions, heart function) concluded:

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Policy-Relevant Considerations: Concentration-Response (C-R)

Across studies evidence <u>continues to support</u> a linear, no-threshold C-R relationship

- The 2009 PM ISA concluded that epidemiologic evidence indicated a linear, no threshold, relationship between short- and long-term PM exposure and health effects
  - Majority of studies focused on PM_{10}
- Recent epidemiologic studies examine C-R relationship in epidemiologic studies of short-term $PM_{2.5}$ exposure and respiratory hospital admissions and emergency department visits, long-term $PM_{2.5}$ exposure and cardiovascular effects (e.g., hypertension), and short- and long-term $PM_{2.5}$ exposure and mortality
  - Additionally, recent studies examining long-term $PM_{2.5}$ exposure and mortality provide initial evidence of a supralinear C-R relationship at lower concentrations

Policy-Relevant Considerations: Populations Potentially at Increased Risk of a PM-related Health Effect (Chapter 12)

- The NAAQS are intended to protect both the population as a whole and those potentially at increased risk for health effects in response to exposure to criteria air pollutants
  - *Are there specific populations and lifestages at increased risk of a PM-related health effect, compared to a reference population?*
- The ISA identified and evaluated evidence for factors that may increase the risk of $PM_{2.5}$-related health effects in a population or lifestage, classifying the evidence into four categories:
  - Adequate evidence; suggestive evidence; inadequate evidence; evidence of no effect
- Conclusions:
  - Adequate: children and nonwhite populations
  - Suggestive: pre-existing cardiovascular and respiratory disease, overweight/obese, genetic variants glutathione pathways, low SES
  - Inadequate: pre-existing diabetes, older adults, residential location, sex, diet, and physical activity

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Welfare Effects: Causality Determinations

Chapter 13. Welfare Effects	2009 PM ISA	Current PM ISA
Visibility	Causal	Causal
Climate Effects	Causal	Causal
Materials Effects	Causal	Causal

Reminder: Ecological effects resulting from the deposition of PM and PM components are being considered as part of the review of the secondary (welfare-based) NAAQS for oxides of nitrogen, oxides of sulfur and PM

Welfare Effects (Chapter 13)

Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between PM and welfare effects

- Visibility Impairment (Causal)
  - Long-term visibility improvements throughout the U.S as PM concentrations have decreased
  - Regional and seasonal patterns in atmospheric visibility parallel PM concentration patterns
  - More evidence supporting the relationship between visibility and PM composition
- Climate Effects (Causal)
  - New evidence provides greater specificity about radiative forcing
  - Increased understanding of additional climate impacts driven by PM radiative effects
  - Improved characterization of key sources of uncertainty particularly with response to PM-cloud interactions
- Materials Effects (Causal)
  - New information for glass and metals including modeling of glass soiling
  - Progress in the development of quantitative dose-response relationships and damage functions for materials in addition to stone, including glass and metals
  - Quantitative research on PM impacts on energy yield from photovoltaic systems

Next Steps for the PM ISA

Awaiting OAR reaction to additional ISA text	
Release draft ISA	**October ASAP, 2018**
Release FRN for public comment	**October ASAP**
CASAC In Place	**Need to finalize ASAP**
CASAC Review meeting	December 12-13, 2018 (tentative)
Public comment opportunity on draft ISA	Until December 12-13, 2018
Revise ISA in response to comments	Winter – Summer 2019
Release Final ISA	December 2019

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Supplemental Materials

ISA Schedules

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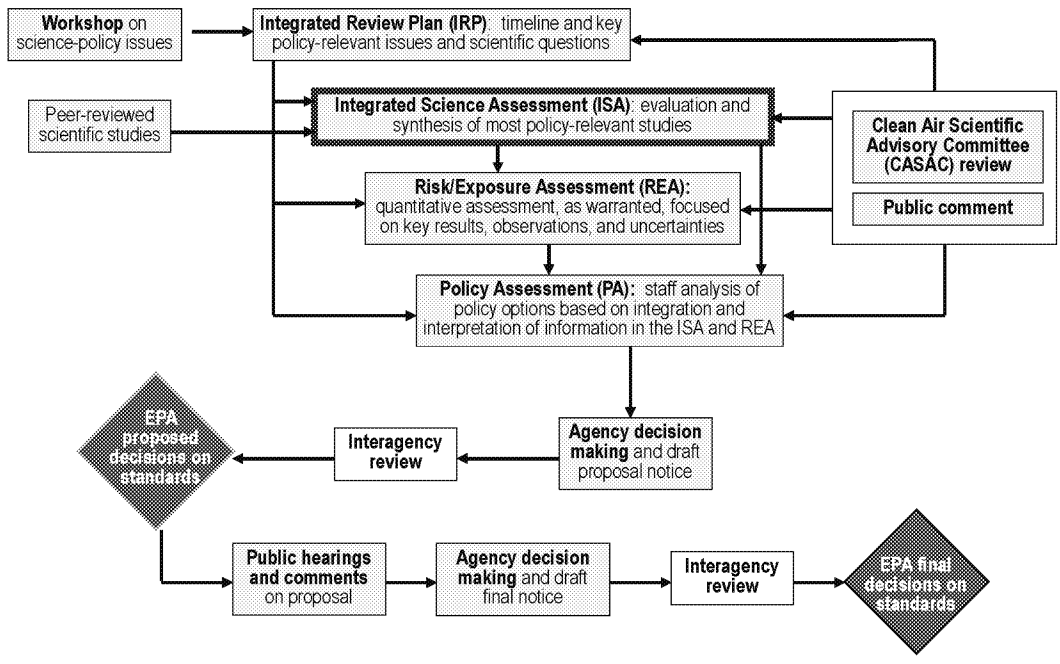
Overview of the NAAQS Review Process



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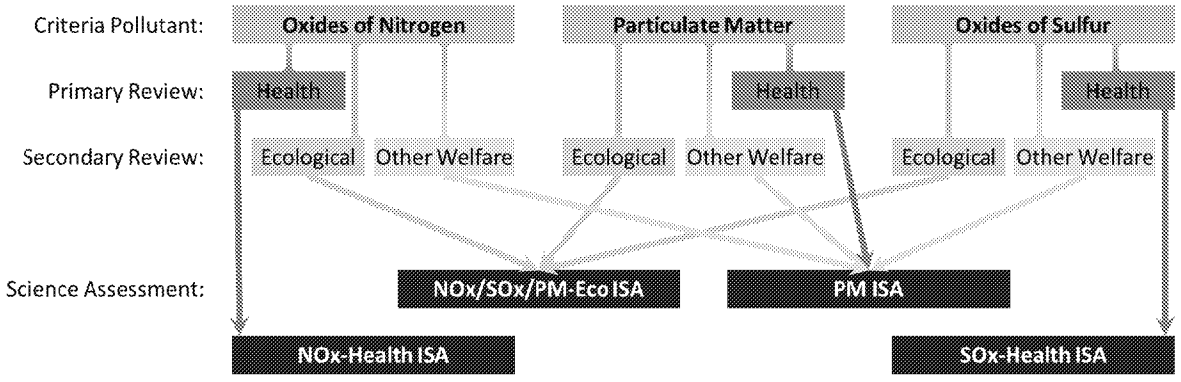
Relationship among Integrated Science Assessments



Notes: Primary (health-based) review of effects on public health = Health
Secondary (welfare-based) review of effects on pubic welfare = Ecological + Other Welfare
Ecological = effects on soil, water, crops, vegetation, animals, wildlife
Other Welfare = effects on manmade materials, weather, visibility, climate

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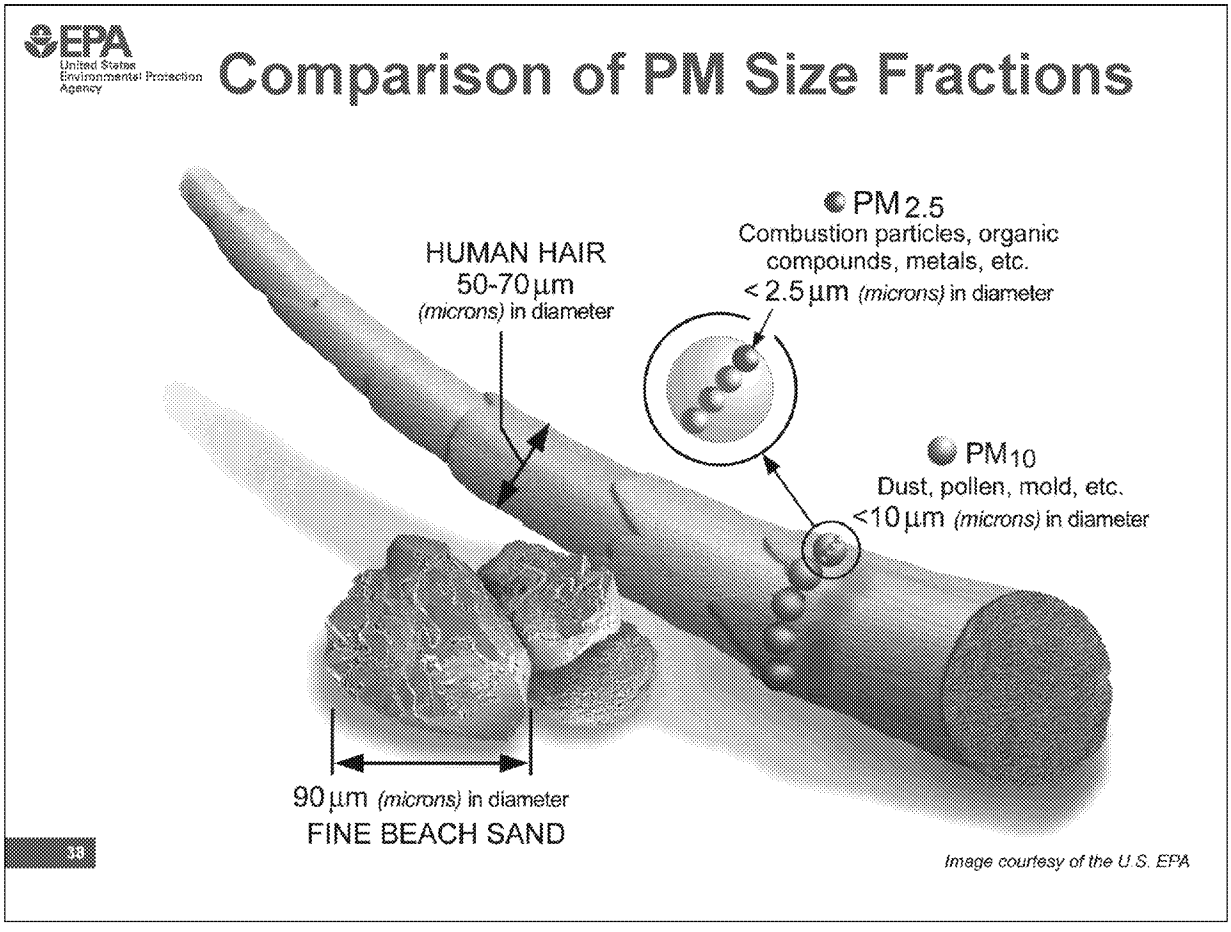
Framework for Causality Determinations

- Consistent and transparent basis to evaluate the likelihood of a causal relationship between air pollution and health or welfare effects
- Based on evaluation and synthesis of evidence from across scientific disciplines (e.g., controlled human exposure, epidemiologic, and toxicological studies)
- Weight-of-evidence approach
  - Causal relationship
  - Likely to be a causal relationship
  - Suggestive of, but not sufficient to infer, a causal relationship
  - Inadequate to infer the presence or absence of a causal relationship
  - Not likely to be a causal relationship
- ISA Preamble describes this framework
  - Stand-alone document, input from CASAC
- Multiple CASAC panels support the use of this framework in ISAs

Current Framework for Causality Determinations

Causal relationship	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures (e.g., doses or exposures generally within one to two orders of magnitude of current levels). That is, the pollutant has been shown to result in health effects in studies in which chance, confounding, and other biases could be ruled out with reasonable confidence. For example: (1) controlled human exposure studies that demonstrate consistent effects; or (2) observational studies that cannot be explained by plausible alternatives or that are supported by other lines of evidence (e.g., animal studies or mode of action information). Generally, the determination is based on multiple high-quality studies conducted by multiple research groups.	Multiple, high-quality studies Rule out chance, confounding, and other biases with reasonable confidence
Likely to be a causal relationship	Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies where results are not explained by chance, confounding, and other biases, but uncertainties remain in the evidence overall. For example: (1) observational studies show an association, but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or (2) animal toxicological evidence from multiple studies from different laboratories demonstrate effects, but limited or no human data are available. Generally, the determination is based on multiple high-quality studies.	Multiple, high-quality studies Important uncertainties remain
Suggestive of, but not sufficient, to infer a causal relationship	Evidence is suggestive of a causal relationship with relevant pollutant exposures but is limited, and chance, confounding and other biases cannot be ruled out. For example, (1) when the body of evidence is relatively small, at least one high-quality epidemiologic study shows an association with a given health outcome and/or at least one high-quality toxicological study shows effects relevant to humans in animal species; or (2) when the body of evidence is relatively large, evidence from studies of varying quality is generally supportive but not entirely consistent, and there may be coherence across lines of evidence (e.g., animal studies or mode of action information) to support the determination.	Evidence is suggestive but limited
Inadequate to infer a causal relationship	Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quantity, quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an effect.	Evidence is of insufficient quantity, quality, consistency, or statistical power
Not likely to be a causal relationship	Evidence indicates there is no causal relationship with relevant pollutant exposures. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering at-risk populations and lifestages, are mutually consistent in not showing an effect at any level of exposure.	Multiple studies show no effect across exposure concentrations


EPA
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Comparison of PM Size Fractions
HUMAN HAIR
50-70 µm
(microns) in diameter
PM2.5
Combustion particles, organic compounds, metals, etc.
< 2.5 µm (microns) in diameter
PM10
Dust, pollen, mold, etc.
<10 µm (microns) in diameter
90 µm (microns) in diameter
FINE BEACH SAND
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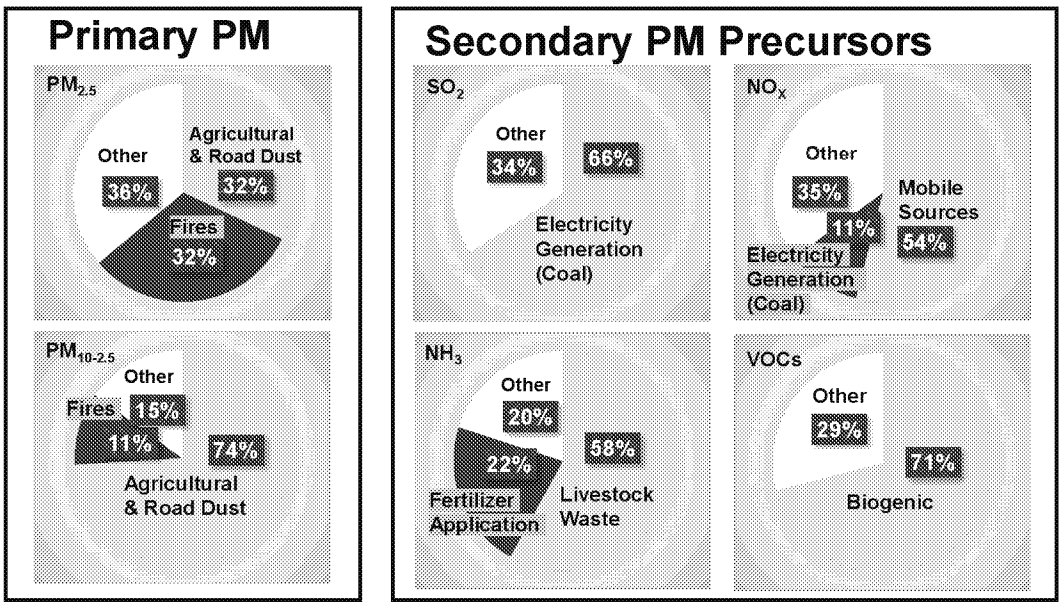
Image courtesy of the U.S. EPA

PM and Precursor Sources (Chapter 2)



- Each precursor has distinctive source or source mixture
- SO_2 emissions decreased from 13.9 million metric tons in 2006 to 4.8 million metric tons in 2014

$PM_{2.5}$ Component Concentrations and Trends (Chapter 2)

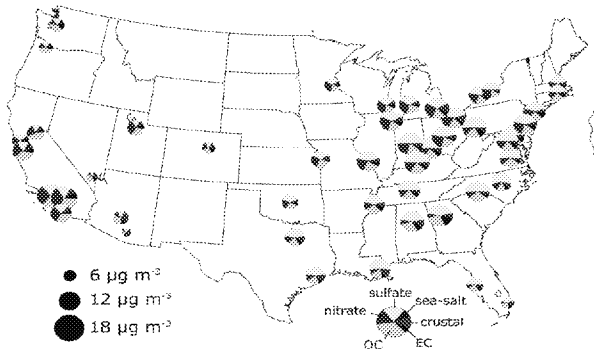


Figure 2-25. 2003 - 2005

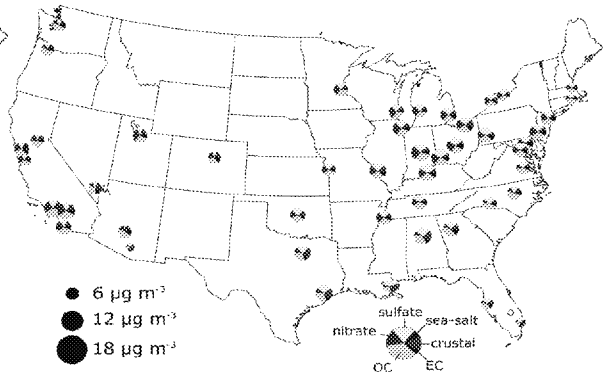
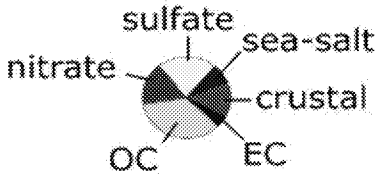


Figure 2-26. 2013 - 2015



- 2003 - 2005: As % of total mass, sulfate higher in East; OC in West
- 2013 – 2015: Reduction in sulfate contribution in East; contributions similar to 2003 – 2005 in West
- Overall: Organic carbon has replaced sulfate as the most abundant component of $PM_{2.5}$ in many locations, specifically in the eastern U.S.
  - Resulting from ~65% reduction in SO_2 emissions

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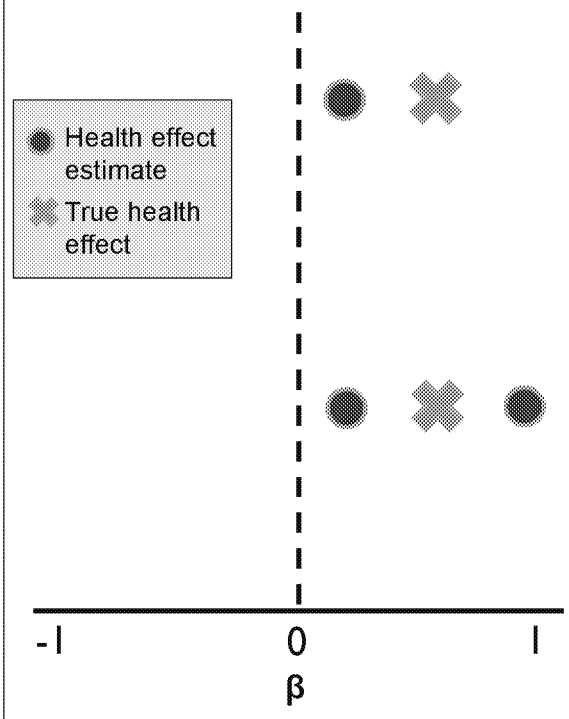
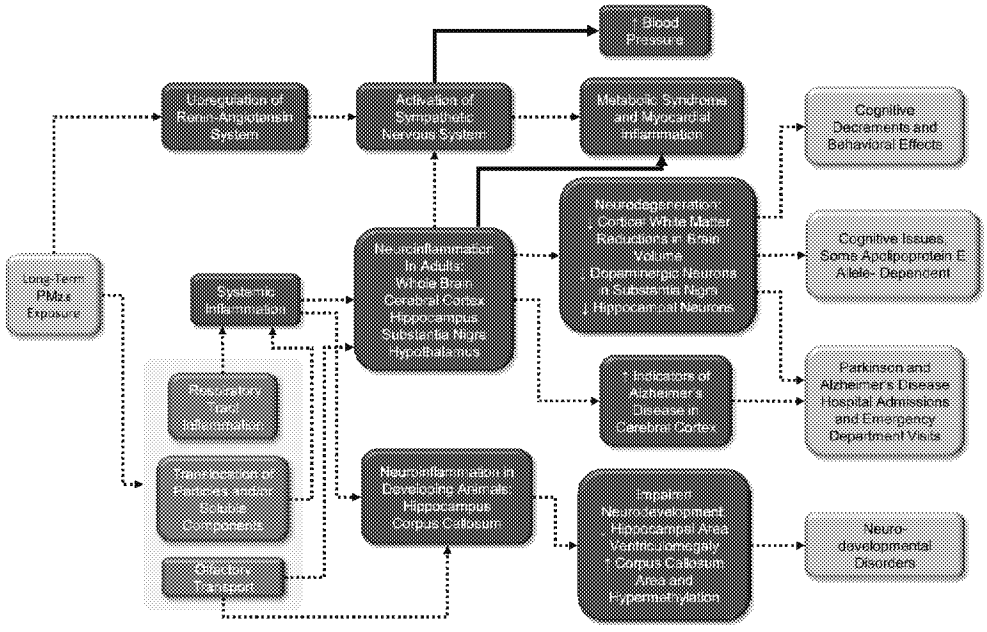
Exposure to PM (Chapter 3)



- **Short-term exposure studies:** exposure error produces underestimation of health effects
  - In this case, we have evidence that the effect exists, and uncertainty is due to the effect being bigger than we estimate
- **Long-term exposure studies:** exposure error produces underestimation or overestimation of health effects
  - Overestimation of health effects occurs if the exposure model has low spatial resolution and underestimates exposures
  - It is necessary to look at the individual study details to determine quality of the exposure assessment

Example: Potential Biological Pathways Figure (Likely to be Causal)



Note: The boxes above represent the effects for which there is experimental or epidemiologic evidence, and the dotted arrows indicate a proposed relationship between those effects. Solid arrows denote direct evidence of the relationship as provided, for example, by an inhibitor of the pathway or a genetic knock-out model used in an experimental study. Shading around multiple boxes denotes relationships between groups of upstream and downstream effects. Progression of effects is depicted from left to right and color-coded (gray, exposure; green, initial event; blue, intermediate event; orange, apical event). Here, apical events generally reflect results of epidemiologic studies, which often observe effects at the population level. Epidemiologic evidence may also contribute to upstream boxes. When there are gaps in the evidence, there are complementary gaps in the figure.

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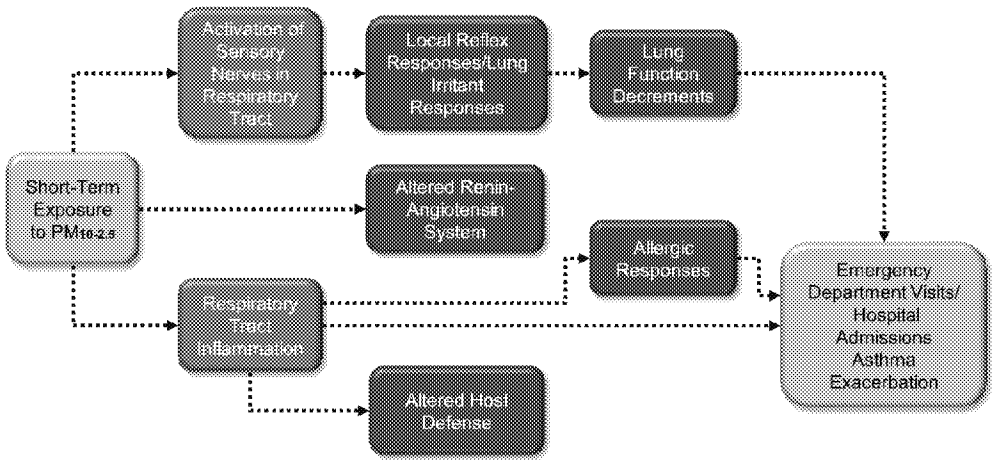
Example: Potential Biological Pathways Figure (Suggestive)



Note: The boxes above represent the effects for which there is experimental or epidemiologic evidence, and the dotted arrows indicate a proposed relationship between those effects. Solid arrows denote direct evidence of the relationship as provided, for example, by an inhibitor of the pathway or a genetic knock-out model used in an experimental study. Shading around multiple boxes denotes relationships between groups of upstream and downstream effects. Progression of effects is depicted from left to right and color-coded (gray, exposure; green, initial event; blue, intermediate event; orange, apical event). Here, apical events generally reflect results of epidemiologic studies, which often observe effects at the population level. Epidemiologic evidence may also contribute to upstream boxes. When there are gaps in the evidence, there are complementary gaps in the figure.

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Health Effects: Causality Determinations

Chapter 5. Respiratory Effects		
Short-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Likely to be Causal	Likely to be Causal
$PM_{10-2.5}$	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
UFP	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Likely to be Causal	Likely to be Causal
$PM_{10-2.5}$	Inadequate	Inadequate
UFP	Inadequate	Inadequate
Chapter 6. Cardiovascular Effects		
Short-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Causal	Causal
$PM_{10-2.5}$	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
UFP	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Causal	Causal
$PM_{10-2.5}$	Inadequate	Suggestive of, but not sufficient to infer
UFP	Inadequate	Inadequate

Red text = new determination or change in causality determination from 2009 PM ISA

Health Effects: Causality Determinations (cont.)

Chapter 7. Metabolic Effects		
Short-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	---	Suggestive of, but not sufficient to infer
$PM_{10-2.5}$	---	Inadequate
UFP	---	Inadequate
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	---	Suggestive of, but not sufficient to infer
$PM_{10-2.5}$	---	Suggestive of, but not sufficient to infer
UFP	---	Inadequate
Chapter 8. Nervous System Effects		
Short-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Inadequate	Suggestive of, but not sufficient to infer
$PM_{10-2.5}$	Inadequate	Inadequate
UFP	Inadequate	Suggestive of, but not sufficient to infer
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	---	Likely to be Causal
$PM_{10-2.5}$	---	Suggestive of, but not sufficient to infer
UFP	---	Likely to be Causal

Red text = new determination or change in causality determination from 2009 PM ISA or new causality determination

Health Effects: Causality Determinations (cont.)

Chapter 9. Reproductive and Developmental Effects		
Male and Female Reproduction and Fertility		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
$PM_{10-2.5}$	Inadequate	Inadequate
UFP	Inadequate	Inadequate
Pregnancy and Birth Outcomes		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
$PM_{10-2.5}$	Inadequate	Inadequate
UFP	Inadequate	Inadequate
Chapter 10. Cancer		
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Suggestive of, but not sufficient to infer	Likely to be Causal
$PM_{10-2.5}$	Inadequate	Suggestive of, but not sufficient to infer
UFP	Inadequate	Inadequate

Red text = new determination or change in causality determination from 2009 PM ISA

Health Effects: Causality Determinations (cont.)

Chapter 11. Mortality		
Short-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Causal	Causal
$PM_{10-2.5}$	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
UFP	Inadequate	Inadequate
Long-term Exposure		
Size Fraction	2009 PM ISA	Current PM ISA
$PM_{2.5}$	Causal	Causal
$PM_{10-2.5}$	Inadequate	Suggestive of, but not sufficient to infer
UFP	Inadequate	Inadequate

Red text = new determination or change in causality determination from 2009 PM ISA

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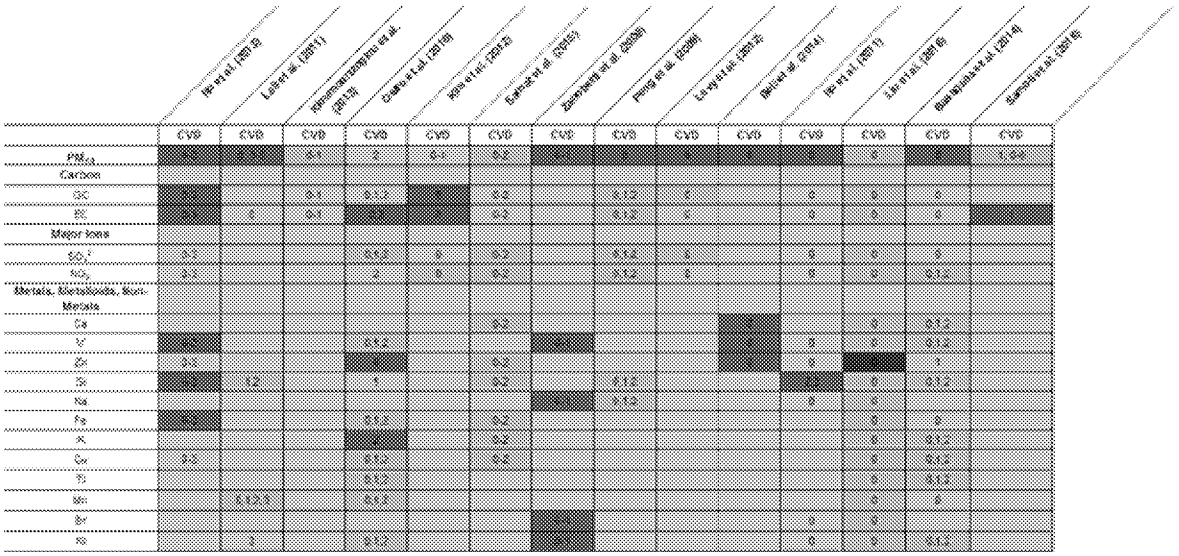
Example: Evaluation of PM Components Studies

Short-term $PM_{2.5}$ and $PM_{2.5}$ Components Exposure and Cardiovascular Effects: Hospital Admissions and Emergency Department (ED) visits – Heat Map



- Numbers represent lags for which associations observed.
- $PM_{2.5}$ mass or $PM_{2.5}$ components associations categorized by results that are statistically significant positive (dark blue), positive/null (light blue), null/negative (light orange), statistically significant negative (red), or not examined (gray).

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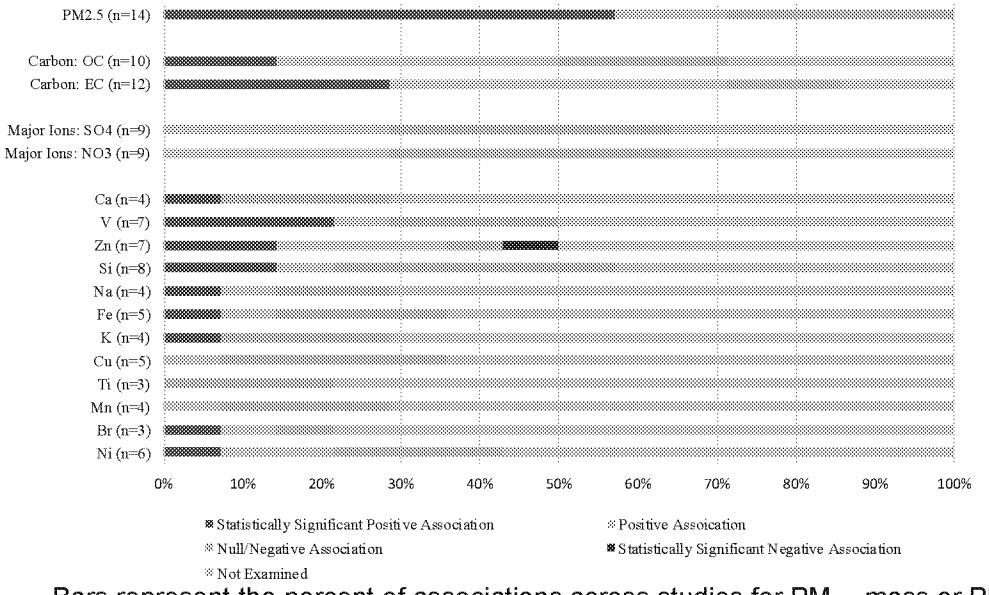
Example: Evaluation of PM Components Studies

Short-term $PM_{2.5}$ and $PM_{2.5}$ Components Exposure and Cardiovascular Effects: Hospital Admissions and ED visits – Distribution of Risk Estimates



Bars represent the percent of associations across studies for $PM_{2.5}$ mass or $PM_{2.5}$ components that are statistically significant positive (dark blue), positive (light blue), null/negative (light orange), statistically significant negative (red), or not examined (gray). n = number of studies that provided an estimate for $PM_{2.5}$ mass and individual $PM_{2.5}$ components.

Overview of Current PM NAAQS

Current Standards					Decisions in 2012 Review
Indicator	**Averaging Time**	**Primary/Secondary**	**Level**	**Form**	
$PM_{2.5}$	Annual	Primary	12.0 µg/m^3	Annual arithmetic mean, averaged over 3 years	Revised level from 15 to 12 µg/m^3*
		Secondary	15.0 µg/m^3		Retained*
	24-hour	Primary and Secondary	35 µg/m^3	98th percentile, averaged over 3 years	Retained
PM_{10}	24-hour	Primary and Secondary	150 µg/m^3	Not to be exceeded more than once per year on average over a 3-year period	Retained

*EPA eliminated spatial averaging for the annual standards

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